```
DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ****** HHHHHHHH SSSSSSSS? ### Status: Signing onto Dialog *******
ENTER PASSWORD:
 ****** HHHHHHHH SSSSSSS? ******
### Status: Login successfulWelcome to DIALOG
Dialog level 05.11.05D
Last logoff: 08may06 15:17:30
Logon file405 11may06 14:19:11
           *** ANNOUNCEMENTS ***
                   ***
NEW FILES RELEASED
***Regulatory Affairs Journals (File 183)
***Index Chemicus (File 302)
***Inspec (File 202)
RESUMED UPDATING
***File 141, Reader's Guide Abstracts
RELOADS COMPLETED
***File 516, D&B--Dun's Market Identifiers
***File 523, D&B European Dun's Market Identifiers
***File 531, American Business Directory
*** MEDLINE has been reloaded with the 2006 MeSH (Files 154 & 155)
*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)
is now available online.
                              ***
DATABASES REMOVED
***File 196, FINDEX
***File 468, Public Opinion Online (POLL)
Chemical Structure Searching now available in Prous Science Drug
Data Report (F452), Prous Science Drugs of the Future (F453),
IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein
Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus
(File 302).
                   ***
 >>>For the latest news about Dialog products, services, content<<<
 >>>and events, please visit What's New from Dialog at <<<
 >>>http://www.dialog.com/whatsnew/. You can find news about <<
 >>>a specific database by entering HELP NEWS <file number>.<<
* * *
SYSTEM: HOME
Cost is in DialUnits
Menu System II: D2 version 1.7.9 term=ASCII
                     *** DIALOG HOMEBASE(SM) Main Menu ***
 Information:
  1. Announcements (new files, reloads, etc.)
  2. Database, Rates, & Command Descriptions
  3. Help in Choosing Databases for Your Topic
  4. Customer Services (telephone assistance, training, seminars, etc.)
  5. Product Descriptions
```

Trying 31060000009999...Open

Connections:

6. DIALOG(R) Document Delivery

- 7. Data Star(R)
  - (c) 2003 Dialog, a Thomson business. All rights reserved.

/H = Help /L = Logoff /NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).

Terminal set to DLINK

\*\*\* DIALOG HOMEBASE(SM) Main Menu \*\*\*

#### Information:

- 1. Announcements (new files, reloads, etc.)
- 2. Database, Rates, & Command Descriptions
- 3. Help in Choosing Databases for Your Topic
- 4. Customer Services (telephone assistance, training, seminars, etc.)
- 5. Product Descriptions

#### Connections:

- 6. DIALOG(R) Document Delivery
- 7. Data Star(R)
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/H = Help /L = Logoff /NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).

? b 155 biosci medline

>>>"MEDLINE" is not a valid category or service name

>>> 44 is unauthorized

>>> 76 is unauthorized

>>>2 of the specified files are not available

11may06 14:19:24 User276629 Session D226.1

\$0.00 0.211 DialUnits FileHomeBase

\$0.00 Estimated cost FileHomeBase

\$0.05 TELNET

\$0.05 Estimated cost this search

\$0.05 Estimated total session cost 0.211 DialUnits

#### SYSTEM:OS - DIALOG OneSearch

File 155:MEDLINE(R) 1951-2006/May 15

(c) format only 2006 Dialog

File 5:Biosis Previews(R) 1969-2006/May W1

(c) 2006 BIOSIS

File 24:CSA Life Sciences Abstracts 1966-2006/Apr

(c) 2006 CSA.

File 28:Oceanic Abstracts 1966-2006/Apr

(c) 2006 CSA.

File 34:SciSearch(R) Cited Ref Sci 1990-2006/Apr W5

(c) 2006 Inst for Sci Info

File 35:Dissertation Abs Online 1861-2006/Apr

(c) 2006 ProQuest Info&Learning

```
File 40:Enviroline(R) 1975-2006/Mar
  File
        41:Pollution Abstracts 1966-2006/Apr
         (c) 2006 CSA.
  File
        50:CAB Abstracts 1972-2006/Apr
         (c) 2006 CAB International
        65:Inside Conferences 1993-2006/May 11
  File
        (c) 2006 BLDSC all rts. reserv.
       71:ELSEVIER BIOBASE 1994-2006/May W1
  File
        (c) 2006 Elsevier Science B.V.
 File
       73:EMBASE 1974-2006/May 11
        (c) 2006 Elsevier Science B.V.
        91:MANTIS(TM) 1880-2006/Feb
 File
        2006 (c) Action Potential
 File
        94:JICST-EPlus 1985-2006/Feb W1
         (c) 2006 Japan Science and Tech Corp(JST)
 File
        98:General Sci Abs 1984-2004/Dec
         (c) 2005 The HW Wilson Co.
  File 110:WasteInfo 1974-2002/Jul
         (c) 2002 AEA Techn Env.
*File 110: This file is closed (no updates)
  File 135: NewsRx Weekly Reports 1995-2006/May W1
         (c) 2006 NewsRx
 File 136:BioEngineering Abstracts 1966-2006/Apr
         (c) 2006 CSA.
 File 143:Biol. & Agric. Index 1983-2006/Apr
         (c) 2006 The HW Wilson Co
  File 144: Pascal 1973-2006/Apr W3
         (c) 2006 INIST/CNRS
  File 164:Allied & Complementary Medicine 1984-2006/May
         (c) 2006 BLHCIS
  File 172: EMBASE Alert 2006/May 11
         (c) 2006 Elsevier Science B.V.
 File 185: Zoological Record Online (R) 1978-2006/May
         (c) 2006 BIOSIS
 File 357: Derwent Biotech Res. 1982-2006/May W1
         (c) 2006 Thomson Derwent & ISI
  File 369:New Scientist 1994-2006/Sep W1
         (c) 2006 Reed Business Information Ltd.
  File 370: Science 1996-1999/Jul W3
         (c) 1999 AAAS
*File 370: This file is closed (no updates). Use File 47 for more current
information.
 File 391:Beilstein Reactions 2006/Q1
         (c) 2005 Beilstein GmbH
 File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
  File 467:ExtraMED(tm) 2000/Dec
         (c) 2001 Informania Ltd.
                                                                       7.
*File 467: F467 will close on February 1, 2006.
      Set Items Description
? s ((crystal or xtal))(30n)((antibody or antibodies))
         1385315 CRYSTAL
              39 XTAL
         2318888 ANTIBODY
         1976907 ANTIBODIES
            6558 ((CRYSTAL OR XTAL))(30N)((ANTIBODY OR ANTIBODIES))
? s sl and (mg/ml)
```

```
>>>Term "ML" is not defined in one or more files
            6558 S1
         3323964 MG/ML
            156 S1 AND (MG/ML)
      S2
>>>Duplicate detection is not supported for File 391.
>>>Records from unsupported files will be retained in the RD set.
             93 RD (unique items)
     s3
? s s3 and py<=1999
Processing
Processed 10 of 29 files ...
Processing
Processed 20 of 29 files ...
>>>One or more prefixes are unsupported
>>> or undefined in one or more files.
Processing
Completed processing all files
             93 S3
       84692606 PY<=1999
            49 S3 AND PY<=1999
     S4
? t s4/ti/all
>>>No matching display code(s) found in file(s): 391
            (Item 1 from file: 155)
```

DIALOG(R) File 155:(c) format only 2006 Dialog. All rts. reserv.

Macromolecular docking of a three-body system: the recognition of human growth hormone by its receptor.

```
(Item 2 from file: 155)
DIALOG(R) File 155:(c) format only 2006 Dialog. All rts. reserv.
```

Quantification of human lithostathine S2-5 forms using the antibody to the N-terminal peptide region.

```
(Item 3 from file: 155)
DIALOG(R) File 155:(c) format only 2006 Dialog. All rts. reserv.
```

Endothelial activation in monosodium urate monohydrate crystal-induced inflammation: in vitro and in vivo studies on the roles of tumor necrosis factor alpha and interleukin-1.

```
4/TI/4
            (Item 4 from file: 155)
DIALOG(R) File 155:(c) format only 2006 Dialog. All rts. reserv.
```

Expression of osteopontin, a urinary inhibitor of stone mineral crystal growth, in rat kidney.

```
(Item 5 from file: 155)
DIALOG(R) File 155:(c) format only 2006 Dialog. All rts. reserv.
```

Conformational analyses on soluble and surface bound osteopontin.

4/TI/6 (Item 6 from file: 155)
DIALOG(R)File 155:(c) format only 2006 Dialog. All rts. reserv.

Nephrocalcin in patients with renal cell carcinoma.

4/TI/7 (Item 7 from file: 155)
DIALOG(R)File 155:(c) format only 2006 Dialog. All rts. reserv.

Recombinant anti-sialidase single-chain variable fragment antibody. Characterization, formation of dimer and higher-molecular-mass multimers and the solution of the crystal structure of the single-chain variable fragment/sialidase complex.

4/TI/8 (Item 8 from file: 155)
DIALOG(R)File 155:(c) format only 2006 Dialog. All rts. reserv.

Characterization of the mammalian toxicity of the crystal polypeptides of Bacillus thuringiensis subsp. israelensis.

4/TI/9 (Item 9 from file: 155)
DIALOG(R)File 155:(c) format only 2006 Dialog. All rts. reserv.

Immunocytochemical localization of pancreatic stone protein in the human digestive tract.

4/TI/10 (Item 1 from file: 5)
DIALOG(R)File 5:(c) 2006 BIOSIS. All rts. reserv.

Study of the methods for immobilization of piezoelectric immunobiosensor

4/TI/11 (Item 2 from file: 5)
DIALOG(R)File 5:(c) 2006 BIOSIS. All rts. reserv.

A NEW APPROACH TO THE DEVELOPMENT OF A REUSABLE PIEZOELECTRIC CRYSTAL BIOSENSOR

4/TI/12 (Item 3 from file: 5)
DIALOG(R)File 5:(c) 2006 BIOSIS. All rts. reserv.

DETECTION OF HUMAN TRANSFERRIN BY THE PIEZOELECTRIC CRYSTAL

4/TI/13 (Item 4 from file: 5)
DIALOG(R)File 5:(c) 2006 BIOSIS. All rts. reserv.

CHARACTERIZATION OF THE MAMMALIAN TOXICITY OF THE CRYSTAL POLYPEPTIDES OF BACILLUS-THURINGIENSIS-SSP-ISRAELENSIS

4/TI/14 (Item 5 from file: 5)
DIALOG(R)File 5:(c) 2006 BIOSIS. All rts. reserv.

AROMATIZATION OF C-19 NORSTEROID IN HUMAN PLACENTA LIVER OVARY AND ADIPOSE TISSUES

4/TI/15 (Item 1 from file: 24)
DIALOG(R)File 24:(c) 2006 CSA. All rts. reserv.

Structure at 2.7 angstrom resolution of the Paracoccus denitrificans two-subunit cytochrome c oxidase complexed with an antibody F sub(V) fragment

4/TI/16 (Item 2 from file: 24)
DIALOG(R)File 24:(c) 2006 CSA. All rts. reserv.

Sensitive titration microcalorimetric study of the binding of Salmonella O-antigenic oligosaccharides by a monoclonal antibody.

4/TI/17 (Item 3 from file: 24)
DIALOG(R)File 24:(c) 2006 CSA. All rts. reserv.

Determination of microbes and immunoglobulins using a piezoelectric biosensor.

4/TI/18 (Item 1 from file: 34)
DIALOG(R) File 34:(c) 2006 Inst for Sci Info. All rts. reserv.

Title: A new method for antibody(antigen) immobilization based on plasma-polymerized film

4/TI/19 (Item 2 from file: 34)
DIALOG(R)File 34:(c) 2006 Inst for Sci Info. All rts. reserv.

Title: Expression, purification, and structural characterization of the bacteriorhodopsin-aspartyl transcarbamylase fusion protein

4/TI/20 (Item 3 from file: 34)
DIALOG(R)File 34:(c) 2006 Inst for Sci Info. All rts. reserv.

Title: Direct determination of etofenprox using surface plasmon resonance

4/TI/21 (Item 4 from file: 34)
DIALOG(R)File 34:(c) 2006 Inst for Sci Info. All rts. reserv.

Title: Single-chain Fv of anti-idiotype 11-1G10 antibody interacts with antibody NC41 single-chain Fv with a higher affinity than the affinity for the interaction of the parent Fab fragments

4/TI/22 (Item 5 from file: 34)
DIALOG(R) File 34:(c) 2006 Inst for Sci Info. All rts. reserv.

Title: Effects of substitutions in the binding surface of an antibody on antigen affinity

4/TI/23 (Item 6 from file: 34)
DIALOG(R) File 34: (c) 2006 Inst for Sci Info. All rts. reserv.

Title: Compared structures of the free nicotinic acetylcholine receptor main immunogenic region (MIR) decapeptide and the antibody-bound [A(76)]MIR analogue: A molecular dynamics simulation from two-dimensional NMR data

4/TI/24 (Item 7 from file: 34)
DIALOG(R)File 34:(c) 2006 Inst for Sci Info. All rts. reserv.

Title: CRYSTALLIZATION OF A DEGLYCOSYLATED T-CELL RECEPTOR (TCR) COMPLEXED WITH AN ANTI-TCR FAB FRAGMENT

4/TI/25 (Item 8 from file: 34)
DIALOG(R) File 34:(c) 2006 Inst for Sci Info. All rts. reserv.

Title: A T-CELL RECEPTOR V-ALPHA DOMAIN EXPRESSED IN BACTERIA - DOES IT DIMERIZE IN SOLUTION

4/TI/26 (Item 9 from file: 34)
DIALOG(R) File 34:(c) 2006 Inst for Sci Info. All rts. reserv.

Title: ANTIBODY-DEPENDENT SIGNAL AMPLIFICATION IN TUMOR XENOGRAFTS AFTER PRETREATMENT WITH BIOTINYLATED MONOCLONAL-ANTIBODY AND AVIDIN OR STREPTAVIDIN

4/TI/27 (Item 10 from file: 34)
DIALOG(R) File 34:(c) 2006 Inst for Sci Info. All rts. reserv.

Title: INTERFERON INDUCTION OF HUMAN TRYPTOPHANYL-TRANSFER-RNA SYNTHETASE SAFEGUARDS THE SYNTHESIS OF TRYPTOPHAN-RICH IMMUNE-SYSTEM PROTEINS - A HYPOTHESIS

4/TI/28 (Item 11 from file: 34)
DIALOG(R)File 34:(c) 2006 Inst for Sci Info. All rts. reserv.

Title: CALMODULIN AS A VERSATILE TAG FOR ANTIBODY FRAGMENTS

4/TI/29 (Item 12 from file: 34)
DIALOG(R) File 34: (c) 2006 Inst for Sci Info. All rts. reserv.

Title: ADSORPTION OF ANTIBODIES TO A LANGMUIR LAYER OF OCTADECYLAMINE AND THE INTERACTION WITH ANTIGEN

4/TI/30 (Item 13 from file: 34)
DIALOG(R)File 34:(c) 2006 Inst for Sci Info. All rts. reserv.

Title: HIGH-LEVEL EXPRESSION IN ESCHERICHIA-COLI AND RAPID PURIFICATION OF ENZYMATICALLY ACTIVE HONEY-BEE VENOM PHOSPHOLIPASE-A2

4/TI/31 (Item 14 from file: 34)
DIALOG(R) File 34:(c) 2006 Inst for Sci Info. All rts. reserv.

Title: 2 APPROACHES TO THE RAPID SCREENING OF CRYSTALLIZATION CONDITIONS

4/TI/32 (Item 1 from file: 35)
DIALOG(R)File 35:(c) 2006 ProQuest Info&Learning. All rts. reserv.

TESTING THE STRUCTURAL BASIS OF THE HYHEL-5/LYSOZYME INTERACTION (SALT BRIDGE, ANTIBODIES)

4/TI/33 (Item 2 from file: 35)
DIALOG(R)File 35:(c) 2006 ProQuest Info&Learning. All rts. reserv.

CHARACTERIZATION OF AN ANTIBODY BINDING SITE BY SITE-DIRECTED MUTAGENESIS AND NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

4/TI/34 (Item 1 from file: 50)
DIALOG(R)File 50:(c) 2006 CAB International. All rts. reserv.

Development of a biosensor to identify toxins using liquid crystal membrane.

4/TI/35 (Item 1 from file: 71)
DIALOG(R)File 71:(c) 2006 Elsevier Science B.V. All rts. reserv.

Semicarbazide-sensitive amine oxidase in pig heart

4/TI/36 (Item 1 from file: 73)
DIALOG(R)File 73:(c) 2006 Elsevier Science B.V. All rts. reserv.

Microbial pest control agent: Bacillus thuringiensis

4/TI/37 (Item 1 from file: 98)
DIALOG(R)File 98:(c) 2005 The HW Wilson Co. All rts. reserv.

Piezoelectric immunosensors for urine specimens of Chlamydia trachomatis employing quartz crystal microbalance microgravimetric analyses.

4/TI/38 (Item 1 from file: 357)
DIALOG(R)File 357:(c) 2006 Thomson Derwent & ISI. All rts. reserv.

Thiolated Salmonella sp. antibody immobilization onto the gold surface of piezoelectric quartz crystal - peroxidase-labeled antibody immobilization on a gold enzyme electrode for Salmonella typhimurium analysis

4/TI/39 (Item 2 from file: 357)
DIALOG(R) File 357: (c) 2006 Thomson Derwent & ISI. All rts. reserv.

Transgenic sweet potato plants resistant to pests: field results Agrobacterium tumefaciens-mediated Bacillus thuringiensis crystal
protein cryIIIA gene transfer and transgenic plant propagation for
insect resistance (conference paper)

4/TI/40 (Item 3 from file: 357)
DIALOG(R)File 357:(c) 2006 Thomson Derwent & ISI. All rts. reserv.

Development of a piezoelectric immunosensor for the detection of enterobacteria - biosensor construction with Escherichia coli antigen mouse monoclonal antibody

4/TI/41 (Item 4 from file: 357)
DIALOG(R)File 357:(c) 2006 Thomson Derwent & ISI. All rts. reserv.

Development of a piezoelectric immunosensor for the detection of Salmonella typhimurium - antibody immobilization onto piezoelectric crystal; biosensor construction

4/TI/42 (Item 5 from file: 357)
DIALOG(R)File 357:(c) 2006 Thomson Derwent & ISI. All rts. reserv.

Piezoelectric crystal biosensor modified with protein A for determination of immunoglobulins - human and mouse IgG analysis

4/TI/43 (Item 6 from file: 357)
DIALOG(R)File 357:(c) 2006 Thomson Derwent & ISI. All rts. reserv.

Expression in Escherichia coli of a cloned crystal protein gene of Bacillus thuringiensis subsp. israelensis - cloning and characterization

4/TI/44 (Item 7 from file: 357)
DIALOG(R)File 357:(c) 2006 Thomson Derwent & ISI. All rts. reserv.

Analysis of human pancreatic juice constitutents related to the pancreatic stone protein using monoclonal antibody - calcium carbonate crystal growth-inhibitor monoclonal antibody preparation using hybridoma

**4/TI/45** (Item 1 from file: 370)
DIALOG(R) File 370: (c) 1999 AAAS. All rts. reserv.

Crystallographic Evidence for Preformed Dimers of Erythropoietin Receptor

# Before Ligand Activation

```
4/TI/46
             (Item 2 from file: 370)
DIALOG(R) File 370: (c) 1999 AAAS. All rts. reserv.
Immunological Origins of Binding and Catalysis in a Diels-Alderase Antibody
 4/TI/47
             (Item 3 from file: 370)
DIALOG(R) File 370: (c) 1999 AAAS. All rts. reserv.
Structural Insights into the Evolution of an Antibody Combining Site
 4/TI/48
             (Item 4 from file: 370)
DIALOG(R) File 370: (c) 1999 AAAS. All rts. reserv.
Structure of the Amino-Terminal Core Domain of the HIV-1 Capsid Protein
 4/TI/49
             (Item 5 from file: 370)
DIALOG(R) File 370: (c) 1999 AAAS. All rts. reserv.
The Immunological Evolution of Catalysis
? logoff
       11may06 14:26:59 User276629 Session D226.2
            $2.39 0.702 DialUnits File155
               $0.00 9 Type(s) in Format 6 (UDF)
            $0.00 9 Types
           Estimated cost File155
     $2.39
            $4.51 0.764 DialUnits File5
               $0.00 5 Type(s) in Format 6 (UDF)
            $0.00 5 Types
           Estimated cost File5
     $4.51
            $1.03
                  0.166 DialUnits File24
               $0.00 3 Type(s) in Format 6 (UDF)
            $0.00 3 Types
           Estimated cost File24
     $1.03
            $0.21
                    0.034 DialUnits File28
     $0.21 Estimated cost File28
           $12.21 0.520 DialUnits File34
               $0.00 14 Type(s) in Format 6 (UDF)
            $0.00 14 Types
    $12.21
           Estimated cost File34
                   0.108 DialUnits File35
            $0.44
               $0.00 2 Type(s) in Format 6 (UDF)
            $0.00 2 Types
            Estimated cost File35
            $0.27
                    0.038 DialUnits File40
     $0.27
           Estimated cost File40
            $0.19
                    0.030 DialUnits File41
           Estimated cost File41
     $0.19
                    0.298 DialUnits File50
            $1.37
               $0.00 1 Type(s) in Format 6 (UDF)
            $0.00 1 Types
     $1.37 Estimated cost File50
            $1.29
                  0.344 DialUnits File65
```

\$1.29 Estimated cost File65

```
$1.06
                0.120 DialUnits File71
          $0.00 1 Type(s) in Format 6 (UDF)
       $0.00 1 Types
$1.06
       Estimated cost File71
                0.486 DialUnits File73
       $5.45
          $0.00 1 Type(s) in Format 6 (UDF)
       $0.00 1 Types
       Estimated cost File73
$5.45
       $0.14
                0.032 DialUnits File91
$0.14
       Estimated cost File91
       $0.71
                0.204 DialUnits File94
$0.71 Estimated cost File94
       $0.36
                0.084 DialUnits File98
          $0.00 1 Type(s) in Format 6 (UDF)
       $0.00 1 Types
$0.36
       Estimated cost File98
                0.028 DialUnits File110
       $0.16
$0.16
       Estimated cost File110
       $0.21
               0.038 DialUnits File135
       Estimated cost File135
$0.21
       $0.19 0.030 DialUnits File136
       Estimated cost File136
$0.19
               0.070 DialUnits File143
       $0.21
$0.21
       Estimated cost File143
       $3.26
               0.724 DialUnits File144
       Estimated cost File144
$3.26
       $0.08
                0.024 DialUnits File164
       Estimated cost File164
$0.08
       $0.18
                0.016 DialUnits File172
       Estimated cost File172
$0.18
       $0.69
                0.112 DialUnits File185
$0.69
       Estimated cost File185
       $2.19
              0.098 DialUnits File357
          $0.00 7 Type(s) in Format 6 (UDF)
       $0.00 7 Types
       Estimated cost File357
       $0.06
                0.016 DialUnits File369
$0.06
       Estimated cost File369
                0.032 DialUnits File370
          $0.00 5 Type(s) in Format 6 (UDF)
       $0.00 5 Types
$0.11
       Estimated cost File370
       $0.00
               0.024 DialUnits File391
$0.00 Estimated cost File391
      $12.92
                0.550 DialUnits File434
       Estimated cost File434
$12.92
                0.016 DialUnits File467
       $0.10
       Estimated cost File467
$0.10
       OneSearch, 29 files, 5.712 DialUnits FileOS
$2.13
       TELNET
$54.12 Estimated cost this search
$54.17 Estimated total session cost 5.922 DialUnits
```

Logoff: level 05.11.05 D 14:26:59

You are now logged offTrying 31060000009999...Open

DIALOG INFORMATION SERVICES

```
PLEASE LOGON:
 ****** HHHHHHHH SSSSSSSS? ### Status: Signing onto Dialog *******
ENTER PASSWORD:
 ****** HHHHHHH SSSSSSS? ******
Welcome to DIALOG
### Status: Login successfulDialog level 05.11.05D
Last logoff: 11may06 14:26:59
Logon file405 12may06 08:26:57
          *** ANNOUNCEMENTS ***
NEW FILES RELEASED
***Regulatory Affairs Journals (File 183)
***Index Chemicus (File 302)
***Inspec (File 202)
RESUMED UPDATING
***File 141, Reader's Guide Abstracts
RELOADS COMPLETED
***File 516, D&B--Dun's Market Identifiers
***File 523, D&B European Dun's Market Identifiers
***File 531, American Business Directory
*** MEDLINE has been reloaded with the 2006 MeSH (Files 154 & 155)
*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)
is now available online.
DATABASES REMOVED
***File 196, FINDEX
***File 468, Public Opinion Online (POLL)
Chemical Structure Searching now available in Prous Science Drug
Data Report (F452), Prous Science Drugs of the Future (F453),
IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein
Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus
(File 302).
>>>For the latest news about Dialog products, services, content<<<
>>>and events, please visit What's New from Dialog at <<<
>>>http://www.dialog.com/whatsnew/. You can find news about <<
>>>a specific database by entering HELP NEWS <file number>.<<
* * *
SYSTEM: HOME
Cost is in DialUnits
Menu System II: D2 version 1.7.9 term=ASCII
                     *** DIALOG HOMEBASE(SM) Main Menu ***
 Information:
  1. Announcements (new files, reloads, etc.)
  2. Database, Rates, & Command Descriptions
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  4. Customer Services (telephone assistance, training, seminars, etc.)
  5. Product Descriptions
 Connections:
  6. DIALOG(R) Document Delivery
  7. Data Star(R)
```

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/H = Help/L = Logoff /NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).

Terminal set to DLINK

\*\*\* DIALOG HOMEBASE(SM) Main Menu \*\*\*

#### Information:

- 1. Announcements (new files, reloads, etc.)
- 2. Database, Rates, & Command Descriptions
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#### Connections:

- 6. DIALOG(R) Document Delivery
- 7. Data Star(R)
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/H = Help/L = Logoff/NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).

? b 155 biosci medicine

44 is unauthorized >>>

76 is unauthorized >>>

>>> 138 is unauthorized

>>>3 of the specified files are not available 12may06 08:27:05 User276629 Session D227.1

0.214 DialUnits FileHomeBase \$0.00

\$0.00 Estimated cost FileHomeBase

\$0.03 TELNET

\$0.03 Estimated cost this search

\$0.03 Estimated total session cost 0.214 DialUnits

# SYSTEM:OS - DIALOG OneSearch

File 155:MEDLINE(R) 1951-2006/May 16

(c) format only 2006 Dialog

5:Biosis Previews (R) 1969-2006/May W1

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24:CSA Life Sciences Abstracts 1966-2006/Apr File

(c) 2006 CSA.

28:Oceanic Abstracts 1966-2006/Apr File

(c) 2006 CSA.

File 34:SciSearch(R) Cited Ref Sci 1990-2006/May W1

(c) 2006 Inst for Sci Info

File 35:Dissertation Abs Online 1861-2006/Apr

(c) 2006 ProQuest Info&Learning

File 40:Enviroline(R) 1975-2006/Mar

File 41:Pollution Abstracts 1966-2006/Apr

(c) 2006 CSA.

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File 50:CAB Abstracts 1972-2006/Apr
         (c) 2006 CAB International
  File
        65:Inside Conferences 1993-2006/May 11
         (c) 2006 BLDSC all rts. reserv.
        71:ELSEVIER BIOBASE 1994-2006/May W1
         (c) 2006 Elsevier Science B.V.
 File
        73:EMBASE 1974-2006/May 12
         (c) 2006 Elsevier Science B.V.
 File
        91:MANTIS(TM) 1880-2006/Feb
         2006 (c) Action Potential
 File
        94:JICST-EPlus 1985-2006/Feb W1
         (c) 2006 Japan Science and Tech Corp(JST)
 File
        98:General Sci Abs 1984-2004/Dec
         (c) 2005 The HW Wilson Co.
 File 110:WasteInfo 1974-2002/Jul
         (c)
             2002 AEA Techn Env.
*File 110: This file is closed (no updates)
 File 135: NewsRx Weekly Reports 1995-2006/May W1
         (c) 2006 NewsRx
 File 136:BioEngineering Abstracts 1966-2006/Apr
         (c) 2006 CSA.
 File 143:Biol. & Agric. Index 1983-2006/Apr
         (c) 2006 The HW Wilson Co
  File 144: Pascal 1973-2006/Apr W3
         (c) 2006 INIST/CNRS
 File 164:Allied & Complementary Medicine 1984-2006/May
         (c) 2006 BLHCIS
 File 172:EMBASE Alert 2006/May 12
         (c) 2006 Elsevier Science B.V.
  File 185:Zoological Record Online(R) 1978-2006/May
         (c) 2006 BIOSIS
  File 357: Derwent Biotech Res. 1982-2006/May W1
         (c) 2006 Thomson Derwent & ISI
  File 369: New Scientist 1994-2006/Feb W4
         (c) 2006 Reed Business Information Ltd.
 File 370:Science 1996-1999/Jul W3
         (c) 1999 AAAS
*File 370: This file is closed (no updates). Use File 47 for more current
information.
  File 391:Beilstein Reactions 2006/Q1
         (c) 2005 Beilstein GmbH
  File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
  File 467:ExtraMED(tm) 2000/Dec
         (c) 2001 Informania Ltd.
*File 467: F467 will close on February 1, 2006.
                                                                        7.
 File 149:TGG Health&Wellness DB(SM) 1976-2006/Apr W4
         (c) 2006 The Gale Group
  File 156:ToxFile 1965-2006/May W2
         (c) format only 2006 Dialog
*File 156: ToxFile has resumed updating with UD20051205.
 File 159: Cancerlit 1975-2002/Oct
         (c) format only 2002 Dialog
*File 159: Cancerlit is no longer updating.
Please see HELP NEWS159.
 File 162:Global Health 1983-2006/Apr
         (c) 2006 CAB International
  File 266: FEDRIP 2005/Dec
         Comp & dist by NTIS, Intl Copyright All Rights Res
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File 399:CA SEARCH(R) 1967-2006/UD=14420
         (c) 2006 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
IPCR/8 classification codes now searchable as IC=. See HELP NEWSIPCR.
  File 444: New England Journal of Med. 1985-2006/Apr W5
         (c) 2006 Mass. Med. Soc.
      Set Items Description
      --- ----
                 _____
? s (therapeutic crystal$)
             0 (THERAPEUTIC CRYSTAL$)
? s (therapeutic crystal?)
             0 (THERAPEUTIC CRYSTAL?)
? rd
>>>Duplicate detection is not supported for File 391.
>>>Records from unsupported files will be retained in the RD set.
              0 RD (unique items)
? s therapeutic(30n)crystal?
Processing
         4176725 THERAPEUTIC
         3874518 CRYSTAL?
           5130 THERAPEUTIC (30N) CRYSTAL?
? rd
>>>Duplicate detection is not supported for File 391.
>>>Records from unsupported files will be retained in the RD set.
Processing - Examined 1200 records
Processing - Examined 3000 records
Processing - Examined 4000 records
Processing - Examined 5000 records
           3491 RD (unique items)
      S5
? s s5 and anitbod?
            3491 S5
            348 ANITBOD?
              0 S5 AND ANITBOD?
      S6
? s s5 and antibod?
            3491 S5
         4023808 ANTIBOD?
            238 S5 AND ANTIBOD?
      s7
? s s7 and dt=rev
>>>One or more prefixes are unsupported
>>> or undefined in one or more files.
             238 S7
                 DT=REV
               0 S7 AND DT=REV
      S8
? s s7 and dt=review
>>>One or more prefixes are unsupported
>>> or undefined in one or more files.
             238 S7
         3036669 DT=REVIEW
             11 S7 AND DT=REVIEW
      59
? t s9/medium/all
           (Item 1 from file: 155)
 9/3/1
DIALOG(R) File 155: MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.
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19856445 PMID: 16381600

Mapping of the active site of proteases in the 1960s and rational design of inhibitors/drugs in the 1990s.

Schechter I

Department of Immunology, The Weizmann Institute of Science, Rehovot 76100, Israel. israel.schechter@weizmann.ac.il

Current protein & peptide science (Netherlands) Dec 2005, 6 (6) p501-12, ISSN 1389-2037--Print Journal Code: 100960529

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

# 9/3/2 (Item 2 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

14028036 PMID: 12447901

# Crystal structures of human antibodies : a detailed and unfinished tapestry of immunoglobulin gene products.

Ramsland Paul A; Farrugia William

Structural Biology Laboratory, The Austin Research Institute, Studley Road, Heidelberg, Victoria 3084, Australia. p.ramsland@ari.unimelb.edu.au Journal of molecular recognition - JMR (England) Sep-Oct 2002, 15 (5) p248-59, ISSN 0952-3499--Print Journal Code: 9004580

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

# 9/3/3 (Item 3 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

13989543 PMID: 12406063

# Optimization of factor VIII replacement therapy: can structural studies help in evading antibody inhibitors?

Spiegel P Clint; Stoddard Barry L

Graduate Program in Biomolecular Structure and Design, University of Washington, Division of Basic Sciences, Fred Hutchinson Cancer Research Center, Seattle 98109, USA.

British journal of haematology (England) Nov 2002, 119 (2) p310-22, ISSN 0007-1048--Print Journal Code: 0372544

Contract/Grant No.: R01 HL62470; HL; NHLBI; T32 G08268; PHS

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

## 9/3/4 (Item 4 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv. PMID: 10398406 12455651 Characterization of protein-glycolipid recognition at the membrane bilayer. Evans S V; Roger MacKenzie C Department of Biochemistry, University of Ottawa, 451 Smyth Road, Ottawa, Ontario, Canada, K1H 8M5. Journal of molecular recognition - JMR (ENGLAND) May-Jun 1999, 12 p155-68, ISSN 0952-3499--Print Journal Code: 9004580 Publishing Model Print Document type: Journal Article; Review Languages: ENGLISH Main Citation Owner: NLM Record type: MEDLINE; Completed 9/3/5 (Item 5 from file: 155) DIALOG(R)File 155:MEDLINE(R) (c) format only 2006 Dialog. All rts. reserv. 11828732 PMID: 9647865 Basic guide to the mechanisms of antiestrogen action. MacGregor J I; Jordan V C Robert H. Lurie Comprehensive Cancer Center, Northwestern University Medical School, Chicago, IL 60611, USA. Pharmacological reviews (UNITED STATES) Jun 1998, 50 (2) p151-96, ISSN 0031-6997--Print Journal Code: 0421737 Contract/Grant No.: P20 CA65764; CA; NCI; R01-CA56143; CA; NCI Publishing Model Print Document type: Journal Article; Review Languages: ENGLISH Main Citation Owner: NLM Record type: MEDLINE; Completed 9/3/6 (Item 6 from file: 155) DIALOG(R)File 155:MEDLINE(R) (c) format only 2006 Dialog. All rts. reserv. 11000124 PMID: 8975283 [Diagnosis and therapy of chronic polyarthritis] Diagnose und Therapie der chronischen Polyarthritis. Leeb B F; Machold K P; Smolen J S II. Medizinische Abteilung, Krankenhaus der Stadt Wien-Lainz, Wien. Aug 1996, 36 (8) p657-62, ISSN 0033-832X--Der Radiologe (GERMANY) Journal Code: 0401257 Print Publishing Model Print Document type: Journal Article; Review ; English Abstract Languages: GERMAN Main Citation Owner: NLM Record type: MEDLINE; Completed

# 9/3/7 (Item 7 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

10982315 PMID: 8796986

## Gouty arthritis and uric acid metabolism.

Wise C M; Agudelo C A

Division of Rheumatology, Allergy, and Immunology, Medical College of Virginia, Richmond 23298, USA.

Current opinion in rheumatology (UNITED STATES) May 1996, 8 (3) p248-54, ISSN 1040-8711--Print Journal Code: 9000851

Publishing Model Print; Comment in Curr Opin Rheumatol. 1996 May;8(3) 235-7; Comment in PMID 8796984

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

## 9/3/8 (Item 8 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

10338711 PMID: 7704521

#### Production and structure of diabodies.

Poljak R J

Center for Advanced Research in Biotechnology, University of Maryland Biotechnology Institute, Rockville 20850.

Structure (London, England) (ENGLAND) Dec 15 1994, 2 (12) p1121-3, ISSN 0969-2126--Print Journal Code: 9418985

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

# 9/3/9 (Item 9 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

09183754 PMID: 1549384

# Allergic fungal sinusitis.

Corey J P

University of Chicago, Pritzker School of Medicine, Illinois.

Otolaryngologic clinics of North America (UNITED STATES) Feb 1992, 25 (1) p225-30, ISSN 0030-6665--Print Journal Code: 0144042

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

## 9/3/10 (Item 1 from file: 24)

DIALOG(R)File 24:CSA Life Sciences Abstracts

(c) 2006 CSA. All rts. reserv.

0002642686 IP ACCESSION NO: 6125823 Prion Diseases: Close to Effective Therapy?

Caughey, Byron; Cashman, Neil R

Nature Reviews: Drug Discovery, v 3, n 10, p 874-884, October 2004

PUBLICATION DATE: 2004

PUBLISHER: Nature Publishing Group, The Macmillan Building 4 Crinan Street

London N1 9XW UK, [mailto:feedback@nature.com],

[URL:http://www.nature.com/]

DOCUMENT TYPE: Journal Article; Review

RECORD TYPE: Abstract LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 1474-1776

FILE SEGMENT: CSA Neurosciences Abstracts

# 9/3/11 (Item 1 from file: 34)

DIALOG(R) File 34: SciSearch(R) Cited Ref Sci (c) 2006 Inst for Sci Info. All rts. reserv.

05787934 Genuine Article#: WX516 No. References: 337

Title: Interleukin-6: Structure-function relationships

Author(s): Simpson RJ (REPRINT); Hammacher A; Smith DK; Matthews JM; Ward LD

Corporate Source: ROYAL MELBOURNE HOSP, LUDWIG INST CANC RES, POB 2008/MELBOURNE/VIC 3050/AUSTRALIA/ (REPRINT); WALTER & ELIZA HALL INST MED RES, /PARKVILLE/VIC 3050/AUSTRALIA/; LUDWIG INST CANC RES, MELBOURNE TUMOUR BIOL BRANCH, JOINT PROT STRUCT LAB/PARKVILLE/VIC 3050/AUSTRALIA/; COOPERAT RES CTR CELLULAR GROWTH FACTORS, /PARKVILLE/VIC 3050/AUSTRALIA/

Journal: PROTEIN SCIENCE, 1997, V6, N5 (MAY), P929-955

ISSN: 0961-8368 Publication date: 19970500

Publisher: CAMBRIDGE UNIV PRESS, 40 WEST 20TH STREET, NEW YORK, NY 10011-4211

Language: English Document Type: **REVIEW** (ABSTRACT AVAILABLE) ? t s9/full/all

# 9/9/1 (Item 1 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

19856445 PMID: 16381600

Mapping of the active site of proteases in the 1960s and rational design of inhibitors/drugs in the 1990s.

Schechter I

Department of Immunology, The Weizmann Institute of Science, Rehovot 76100, Israel. israel.schechter@weizmann.ac.il

Current protein & peptide science (Netherlands) Dec 2005, 6 (6) p501-12, ISSN 1389-2037--Print Journal Code: 100960529

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

For several decades the specificity of proteases has been presented as an active site divided into subsites, using the nomenclature of Schechter & Berger from 1967 (S1, S2... for subsites of the active site; P1, P2... for residues of the substrate occupying the corresponding subsites). At early stages of the research (1960s) it was realized that the size of the active site was larger than expected and important interactions occur in regions

remote from the catalytic site. Since the active site was found to be large it was divided into subsites, and a procedure to map it up was developed. The map provides information on the size of the active site (number of subsites), the properties of each subsite (free energy of ligand binding, nature of binding forces, etc.), and it enables rational design of new substrates and inhibitors. Already in 1968 inhibitors with binding ten thousand fold higher than available inhibitors, were constants prepared. The model of a large active site was initially met with strong opposition. Before long, however, predictions of the model (size of the active site, interactions in subsites remote from the catalytic site) were confirmed by X-ray crystallography (1970). During the 1990s proteolytic enzymes received renewed attention in biology and medicine, they became therapeutic targets, and protease inhibitors were successfully applied in the treatment of AIDS and hypertension. The model of large active site divided into subsites, proposed 38 years ago, stood the test of time. This model is still in use in basic research to evaluate enzyme activity, and in pharmaceutical research for the development of inhibitors/drugs. (50 Refs.)

\*Antibodies --chemistry--CH; \*Peptide Hydrolases; \*Peptide Descriptors: Inhibitors--chemistry--CH; Animals; Antibodies Mapping; \*Protease --pharmacology--PD; Binding Sites; Crystallography, X-Ray; Drug Design; Hydrolases--chemistry--CH; Peptide Hydrolases--metabolism--ME; Protease Inhibitors--pharmacology--PD; Structure-Activity Relationship

CAS Registry No.: 0 (Antibodies); 0 (Protease Inhibitors)

Enzyme No.: EC 3.4.-(Peptide Hydrolases)

Record Date Created: 20051229 Record Date Completed: 20060206

#### 9/9/2 (Item 2 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

14028036 PMID: 12447901

Crystal structures of human antibodies : a detailed and unfinished tapestry of immunoglobulin gene products.

Ramsland Paul A; Farrugia William

Structural Biology Laboratory, The Austin Research Institute, Studley Road, Heidelberg, Victoria 3084, Australia. p.ramsland@ari.unimelb.edu.au Journal of molecular recognition - JMR (England) Sep-Oct 2002, 15 (5) p248-59, ISSN 0952-3499--Print Journal Code: 9004580

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Sequencing of all human immunoglobulin (Ig) germline gene segments has recently been completed. However, our first glimpses of the recombined products of this combinatorial gene system were in the 1970s, in landmark publications, reporting the crystal structures of two human myeloma proteins, the Mcg lambda light chain dimer and the New IgG1(lambda) Fab. Although numerous crystal structures of murine and human antibodies have now been determined, only a relatively small proportion of the human germline genes have had their corresponding protein three-dimensional structures resolved. Therefore, further structural investigations are required before the inherent diversity of the antibody repertoire can be fully appreciated. We discuss the detailed structural information available antibodies with regard to their immune functions. Also for human

discussed, is how the structural information is finding application in the 'humanization' of murine **antibodies** as part of their development as 'biopharmaceuticals' for the treatment of human disease. Copyright 2002 John Wiley & Sons, Ltd. (102 Refs.)

Descriptors: \*Immunoglobulins--chemistry--CH; \*Immunoglobulins--genetics --GE; Animals; Antibodies , Monoclonal--chemistry--CH; Antibodies , Monoclonal--genetics--GE; Antibodies , Monoclonal-- therapeutic use--TU; Antibody Diversity; Binding Sites, Antibody; Crystallography , X-Ray; Genes, Immunoglobulin; Humans; Immunoglobulin Constant Regions--chemistry --CH; Immunoglobulin Constant Regions--genetics--GE; Immunoglobulin Variable Region--chemistry--CH; Immunoglobulin Variable Region--genetics--GE; Mice; Models, Molecular; Molecular Structure; Protein Engineering; Protein Structure, Tertiary

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Binding Sites, Antibody); 0 (Immunoglobulin Constant Regions); 0 (Immunoglobulin Variable Region); 0 (Immunoglobulins)

Record Date Created: 20021126
Record Date Completed: 20030617

# 9/9/3 (Item 3 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

13989543 PMID: 12406063

Optimization of factor VIII replacement therapy: can structural studies help in evading antibody inhibitors?

Spiegel P Clint; Stoddard Barry L

Graduate Program in Biomolecular Structure and Design, University of Washington, Division of Basic Sciences, Fred Hutchinson Cancer Research Center, Seattle 98109, USA.

British journal of haematology (England) Nov 2002, 119 (2) p310-22, ISSN 0007-1048--Print Journal Code: 0372544

Contract/Grant No.: R01 HL62470; HL; NHLBI; T32 G08268; PHS

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

(100 Refs.)

Tags: Male

Descriptors: \*Factor VIII--therapeutic use--TU; \*Hemophilia A --drug therapy--DT; Animals; Blood Coagulation Factor Inhibitors--metabolism--ME; Crystallography , X-Ray; Dogs; Epitopes; Factor VIII--chemistry--CH; Factor VIII--immunology--IM; Hemophilia A--immunology--IM; Humans; Mice; Mutation; Recombinant Proteins-- therapeutic use--TU; Research Support, U.S. Gov't, P.H.S.; Sequence Homology; Structure-Activity Relationship; Swine

CAS Registry No.: 0 (Blood Coagulation Factor Inhibitors); 0 (Epitopes); 0 (Recombinant Proteins); 9001-27-8 (Factor VIII)

Record Date Created: 20021030
Record Date Completed: 20021217

# 9/9/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

12455651 PMID: 10398406

Characterization of protein-glycolipid recognition at the membrane bilayer.

Evans S V; Roger MacKenzie C

Department of Biochemistry, University of Ottawa, 451 Smyth Road, Ottawa, Ontario, Canada, K1H 8M5.

Journal of molecular recognition - JMR (ENGLAND) May-Jun 1999, 12 (3) p155-68, ISSN 0952-3499--Print Journal Code: 9004580

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

A growing number of important molecular recognition events are being shown to involve the interactions between proteins and glycolipids. Glycolipids are molecules in which one or more monosaccharides are glycosidically linked to a lipid moiety. The lipid moiety is generally buried in the cell membrane or other bilayer, leaving the oligosaccharide moiety exposed but in close proximity to the bilayer surface. This presents a unique environment for protein-carbohydrate interactions, and studies to determine the influence of the bilayer on these phenomena are in their infancy. One important property of the bilayer is the ability to orient and cluster glycolipid species, as strong interactions in biological systems are often achieved through multivalency arising from the simultaneous association of two or more proteins and receptors. This is especially true of protein-carbohydrate binding because of the unusually low affinities that characterize the monovalent interactions. More recent studies have also shown that the composition of the lipid bilayer is a critical parameter in protein-glycolipid recognition. The fluidity of the bilayer allows for correct geometric positioning of the oligosaccharide head group relative to the binding sites on the protein. In addition, there are activity-based and structural data demonstrating the impact of the bilayer microenvironment on the modulation of oligosaccharide presentation. The use of model membranes in biosensor-based methods has supplied decisive evidence of the importance of the membrane in receptor presentation. These data can be correlated with three-dimensional structural information from X-ray crystallography, NMR, and molecular mechanics to provide insight into specific protein-carbohydrate inter--actions at the bilayer. Copyright 1999 National Research Council Canada and John Wiley & Sons, Ltd. (92 Refs.) Descriptors: \*Glycolipids--metabolism--ME; \*Lipid Bilayers--chemistry--CH

Lipids--metabolism--ME; \*Protein Binding; Antibodies , \*Membrane Monoclonal -- chemistry -- CH; Antibodies , Monoclonal--immunology--IM; Antibodies , Monoclonal--metabolism--ME; Antibodies , Monoclonal-use--TU; Antigen- Antibody Reactions; Bacterial Toxins therapeutic --chemistry--CH; Bacterial Toxins--metabolism--ME; Binding Sites; Carbohydrate Conformation; Carbohydrate Metabolism; Carbohydrate Sequence; Carbohydrates--chemistry--CH; Crystallography , X-Ray; Gangliosides Gangliosides--metabolism Gangliosides--immunology--IM; --chemistry--CH; Glycosphingolipids--chemistry--CH; Glycolipids--chemistry--CH; Glycosphingolipids--metabolism--ME; Humans; Immunotherapy; Liposomes; Macromolecular Substances; Magnetic Resonance Spectroscopy; Melanoma--therapy--TH; Membrane Lipids--chemistry--CH; Models, Molecular; Molecular Sequence Data; Proteins--chemistry--CH; Proteins--metabolism--ME I; Structure-Activity Relationship; Substrate Shiga-Like Toxin Specificity; Surface Plasmon Resonance; Trihexosylceramides--chemistry--CH; Trihexosylceramides--metabolism--ME

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Bacterial Toxins); 0 (Carbohydrates); 0 (Gangliosides); 0 (Glycolipids); 0

(Glycosphingolipids); 0 (Lipid Bilayers); 0 (Liposomes); 0 (Macromolecular Substances); 0 (Membrane Lipids); 0 (Proteins); 0 (Shiga-Like Toxin I); 0 (Trihexosylceramides); 62010-37-1 (ganglioside, GD3); 71965-57-6 (globotriaosylceramide)

Record Date Created: 20000307
Record Date Completed: 20000307

# 9/9/5 (Item 5 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

11828732 PMID: 9647865

Basic guide to the mechanisms of antiestrogen action.

MacGregor J I; Jordan V C

Robert H. Lurie Comprehensive Cancer Center, Northwestern University Medical School, Chicago, IL 60611, USA.

Pharmacological reviews (UNITED STATES) Jun 1998, 50 (2) p151-96,

ISSN 0031-6997--Print Journal Code: 0421737

Contract/Grant No.: P20 CA65764; CA; NCI; R01-CA56143; CA; NCI

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed Subfile: INDEX MEDICUS; Toxbib

Forty years ago, Lerner and coworkers (1958) discovered the first nonsteroidal antiestrogen and Jensen (Jensen and Jacobson, 1960) identified a target for drug action, the ER. This knowledge opened the door for the clinical development of tamoxifen which we now know provides a survival advantage in both node-positive and node-negative patients with ER-positive disease (Early Breast Cancer Trialists Collaborative Group, 1992, 1998). The drug has been studied extensively, and the results have provided an invaluable insight into possible ancillary advantages of "antiestrogens", i.e., maintenance of bone density and the prevention of coronary heart disease, and possible disadvantages, i.e., rat liver carcinogenesis and an increased risk of endometrial cancer. Most importantly, the identification of the target site-specific actions of tamoxifen caused a paradigm shift in the prospective uses of antiestrogens from a direct exploitation of the antitumor properties to the broader application as a preventative for osteoporosis, but with the beneficial side effects of preventing breast and endometrial cancer. Raloxifene, a second-generation SERM, has all the properties in the laboratory that would encourage development as a safe for osteoporosis (Jordan et al., 1997). As a result, preventative raloxifene has been evaluated in more than 11,000 postmenopausal women and found to maintain bone density with significant decreases in breast cancer incidence and no increase in endometrial thickness. Raloxifene is now available as a preventative for osteoporosis in postmenopausal women. There is every reason to believe that a multifaceted agent like raloxifene will find widespread use, and there will be continuing interest by the pharmaceutical industry in the development of new agents with even broader applications. The extensive clinical effort is augmented by past molecular innovations in the laboratory and the future promise of new discoveries. The cloning and sequencing of the ER (Green et al., 1986; Greene et al., 1986) has allowed the development of an ER knock-out mouse (Lubahn et al., 1993) that compliments Jensen's pioneering work (Jensen and Jacobson, 1962) and describes the consequences of the loss of ER alpha. However, ER beta (Kuiper et al., 1996), the second ER, has provided an additional dimension to the description of estrogen and antiestrogen action. For the future, the

development of ER beta monoclonal antibodies , the classification of target sites for the protein around the body, and the creation of ER beta and ER alpha, beta knock-out mice will identify new therapeutic targets modulate physiological functions. Clearly, the successful crystallization of ER alpha with raloxifene (Brzozowski et al., 1997) must act as a stimulus for the crystallization of ER beta. The central issue for research on antiestrogen pharmacology is the discovery of the mechanism (or mechanisms) of target site-specificity for the modulation of estrogenic and antiestrogenic response. The description of a stimulatory pathway for antiestrogens through an AP-1 ER beta signal transduction pathway (Paech et al., 1997), although interesting, may not entirely explain the estrogenicity of antiestrogens. The model must encompass the sum of pharmacological consequences of signal transduction through ER alpha and ER beta with the simultaneous competition from endogenous estrogens at both sites. This is complicated because estradiol is an antagonist at ER beta through AP-1 sites (Paech et al., 1997), so this is clearly not the pathway for estrogen-induced bone maintenance in women. Estrogen is stimulatory through ER alpha, but antiestrogens are usually partial agonists and may either block or stimulate genes. However, we suggest that the ER alpha stimulatory pathway could be amplified through selective increases in coactivators. The principle is illustrated with the MDA-MB-231 cells stably transfected with the cDNAs for the wild-type and the amino acid 351 mutan (539 Refs.)

Descriptors: \*Estrogen Antagonists--pharmacology--PD; Animals; Cell Cycle --drug effects--DE; Estrogen Antagonists--classification--CL; Estrogen Antagonists--therapeutic use--TU; Growth Substances--physiology--PH; Humans; Receptors, Estrogen--drug effects--DE; Receptors, Estrogen--physiology--PH; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.; Tamoxifen--pharmacology--PD

CAS Registry No.: 0 (Estrogen Antagonists); 0 (Growth Substances); 0 (Receptors, Estrogen); 10540-29-1 (Tamoxifen)

Record Date Created: 19980915
Record Date Completed: 19980915

# 9/9/6 (Item 6 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

11000124 PMID: 8975283

# [Diagnosis and therapy of chronic polyarthritis]

Diagnose und Therapie der chronischen Polyarthritis.

Leeb B F; Machold K P; Smolen J S

II. Medizinische Abteilung, Krankenhaus der Stadt Wien-Lainz, Wien.

Der Radiologe (GERMANY) Aug 1996, 36 (8) p657-62, ISSN 0033-832X--Print Journal Code: 0401257

Publishing Model Print

Document type: Journal Article; Review ; English Abstract

Languages: GERMAN

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Rheumatoid arthritis (RA) is the most frequent inflammatory joint disease, and it affects about 1% of the population. The onset of arthritis is rarely acute; it is subacute and usually progresses slowly. The clinical picture of RA is variable: mild to very aggressive and destructive courses, sometimes accompanied by organ involvement, leading to severe functional impairment and early disability can be observed. RA is diagnosed according

to the ACR criteria published in 1958 and modified in 1988. The appearance of a palpable joint swelling or effusion is obligatory for the clinical diagnosis of arthritis. In RA, typically involvement of the joint of the hands and feet can be seen. Laboratory parameters play an important role as both diagnostic and prognostic tools. Besides clinical features and laboratory parameters, imaging techniques provide another cornerstone in the diagnosis of RA. Until now plain X-rays, which primarily visualize osseous changes, are the most important technique in daily practice, whereas magnetic resonance imaging and ultrasound may provide information about soft tissue changes in an earlier stage of disease. The main differential diagnoses of RA to be considered are the seronegative (psoriatic arthritis, arthritides accompanying spondylarthropathies inflammatory bowel diseases, Reiter's syndrome, and spondylitis ankylosans with peripheral arthritis), Parvovirus-induced arthritis, crystal -induced septic arthritis. Early diagnosis and therapeutic arthritides and intervention seem to be of great prognostic importance. In several independently performed investigations a higher mortality was found in RA patients than in the normal population. Drug therapy of RA consists of (NSAIDs), drugs corticosteroids nonsteroidal antirheumatic disease-modifying drugs (DMARDs). When the functional and radiological parameters were assessed, the DMARDs were found to have a disease modifying and in rare cases a remission-inducing property. Moreover, tolerance these to drugs is limited. Newer therapeutic trials have employed substances like bacterial extracts, antibiotics and biological Leflunomid, Tenidap, subcomes (e.g., monoclonal antibodies against cytokines, fusion proteins cytokinereceptors). Some promising results of these soluble investigations need confirmation in larger patient populations, but some new perspectives for a more efficacious treatment of RA can be expected. 21 Refs.)

Descriptors: \*Arthritis, Rheumatoid--diagnosis--DI; \*Diagnostic Imaging; Antirheumatic Agents--therapeutic use--TU; Arthritis, Rheumatoid --drug therapy--DT; Arthritis, Rheumatoid--etiology--ET; Diagnosis, Differential; English Abstract; Humans; Joints--drug effects--DE; Joints--pathology--PA

CAS Registry No.: 0 (Antirheumatic Agents)

Record Date Created: 19961227
Record Date Completed: 19961227

# 9/9/7 (Item 7 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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10982315 PMID: 8796986

Gouty arthritis and uric acid metabolism.

Wise C M; Agudelo C A

Division of Rheumatology, Allergy, and Immunology, Medical College of Virginia, Richmond 23298, USA.

Current opinion in rheumatology (UNITED STATES) May 1996, 8 (3) p248-54, ISSN 1040-8711--Print Journal Code: 9000851

Publishing Model Print; Comment in Curr Opin Rheumatol. 1996 May;8(3) 235-7; Comment in PMID 8796984

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Important observations have continued to expand our understanding of gout. The increased risk of gout in black Americans has been linked more closely with the development of hypertension, and an increasing prevalence

in African blacks and in England may have a similar association, possibly through the use of diuretics. The association of gout and insulin resistance appears to be related to fat distribution, and the link with hyperlipidemia may be related to genetic factors. The relationship between gout and renal disease and the frequency of gout in patients with renal failure continue to be areas of controversy. The mechanism and a possible approach to the hyperuricemia associated with cyclosporine therapeutic therapy are better understood. The potential for antibodies against urate to potentiate further crystallization may explain some of the crystals uncertainties about gouty attacks. Unusual manifestations of gout, including more cases of spinal involvement, were reported. The role of formalin in dissolving urate crystals in pathologic specimens was further clarified, and the use of atomic force microscopy to detect crystals was reported. Corticosteroids are increasingly accepted in treating acute gout, and the role of colchicine in acute and intercritical gout has come under increasing scrutiny. Urate-lowering drugs appear to be cost effective in patients with more than one or two attacks per year. (54 Refs.)

Descriptors: \*Arthritis, Gouty--metabolism--ME; \*Uric Acid--metabolism --ME; Arthritis, Gouty--physiopathology--PP; Arthritis, Gouty--therapy--TH; Humans

CAS Registry No.: 69-93-2 (Uric Acid)

Record Date Created: 19961121
Record Date Completed: 19961121

# 9/9/8 (Item 8 from file: 155)

DIALOG(R) File 155: MEDLINE(R)

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10338711 PMID: 7704521

Production and structure of diabodies.

Poljak R J

Center for Advanced Research in Biotechnology, University of Maryland Biotechnology Institute, Rockville 20850.

Structure (London, England) (ENGLAND) Dec 15 1994, 2 (12) p1121-3, ISSN 0969-2126--Print Journal Code: 9418985

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

The first **crystal** structure of a diabody, a bivalent **antibody** fragment, confirms previous predicted structures and techniques for generating bispecific bivalent **antibody** fragments of considerable **therapeutic** potential. (11 Refs.)

Descriptors: \*Immunoglobulin Fragments--biosynthesis--BI; Amino Acid Sequence; Binding Sites, **Antibody**; Hybridomas; Immunoglobulin Fragments--chemistry--CH; Immunoglobulin Fragments--immunology--IM; Immunoglobulin Variable Region; Molecular Sequence Data; Protein Conformation; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.

CAS Registry No.: 0 (Binding Sites, Antibody); 0 (Immunoglobulin Fragments); 0 (Immunoglobulin Variable Region)

Record Date Created: 19950511
Record Date Completed: 19950511

# 9/9/9 (Item 9 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

09183754 PMID: 1549384

Allergic fungal sinusitis.

Corey J P

University of Chicago, Pritzker School of Medicine, Illinois.

Otolaryngologic clinics of North America (UNITED STATES) Feb 1992, 25

(1) p225-30, ISSN 0030-6665--Print Journal Code: 0144042

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

In summary, AFS is a newly recognized form of sinusitis, appearing in otherwise healthy young adults with a history of chronic bacterial or polypoid rhinosinusitis refractory to conventional therapy. Radiologic study may show patchy opacification or calcifications of the sinuses on CT. The patients have an elevated total IgE, peripheral eosinophilia, and positive skin tests for fungal antigens. They may also have elevated serum fungal allergen-specific IgE and IgG and precipitating antibodies to Aspergillus, Curvularia, or other fungi. Diagnostic and therapeutic surgical drainage of the sinuses will establish a definitive diagnosis by identifying the typical allergic mucin with eosinophils, Charcot-Leyden crystals , few fungal hyphae on silver stain, and a lack of tissue invasion. Treatment, other than surgical drainage, consists of systemic corticosteroids to prevent recurrence of disease. (32 Refs.)

Descriptors: \*Mycoses--diagnosis--DI; \*Respiratory Hypersensitivity --diagnosis--DI; \*Sinusitis--diagnosis--DI; Aspergillosis--complications --CO; Aspergillosis--diagnosis--DI; Aspergillosis--therapy--TH; Diagnosis, Differential; Humans; Mycoses--complications--CO; Mycoses--therapy--TH; Respiratory Hypersensitivity--etiology--ET; Respiratory Hypersensitivity --therapy--TH; Sinusitis--etiology--ET; Sinusitis--therapy--TH

Record Date Created: 19920422 Record Date Completed: 19920422

9/9/10 (Item 1 from file: 24)

DIALOG(R)File 24:CSA Life Sciences Abstracts

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0002642686 IP ACCESSION NO: 6125823 Prion Diseases: Close to Effective Therapy?

Caughey, Byron; Cashman, Neil R

Nature Reviews: Drug Discovery, v 3, n 10, p 874-884, October 2004

PUBLICATION DATE: 2004

PUBLISHER: Nature Publishing Group, The Macmillan Building 4 Crinan Street

London N1 9XW UK, [mailto:feedback@nature.com],

[URL:http://www.nature.com/]

DOCUMENT TYPE: Journal Article; Review

RECORD TYPE: Abstract LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 1474-1776 DOI: 10.1038/nrd1525

#### **ABSTRACT:**

The transmissible spongiform encephalopathies could represent a new mode of transmission for infectious diseases: a process more akin to crystallization than to microbial replication. The prion hypothesis proposes that the normal isoform of the prion protein is converted to a disease-specific species by template-directed misfolding. Therapeutic and prophylactic strategies to combat these diseases have emerged from immunological and chemotherapeutic approaches. The lessons learned in treating prion disease will almost certainly have an impact on other diseases that are characterized by the pathological accumulation of misfolded proteins. Prions represent a new class of infectious agents which propagate on a protein-only level, not requiring agent-encoded nucleic acids. Newly emergent prion diseases such as bovine spongiform encephalopathy, variant Creutzfeldt-Jakob disease (CJD), and chronic wasting disease are a source of critical concern to physicians, veterinarians, economists, politicians : and the general public. Numerous strategies and targets have been proposed for the immunotherapy of prion diseases, based on the necessity of agent replication in lymphoid tissue prion to neuro-invasion, and the sensitivity of prion propagation to antibodies in vitro. Prion replication in cell lines in vitro is sensitive to antibodies directed against the normal and abnormal isoforms of the prion protein. Numerous strategies and potential targets for treating transmissible spongiform encephalopathies have been suggested, with the most studied target being the inhibition of PrP super(Sc) accumulation. The development of higher-throughput screening assays based on scrapie-infected cell cultures have been developed and have greatly accelerated the pace of discovery of PrP super(Sc) inhibitors. Several classes of inhibitors of PrP super(Sc) formation have been identified, some of which show prophylactic activity against scrapie in rodents. However, chemotherapeutic treatments of clinically affected scrapie-infected rodents and CJD-infected humans have been largely ineffectual. Compounds that destabilize PrP super(Sc) and/or reduce scrapie infectivity have been identified that could be useful as decontaminants. The most effective therapeutic strategies might require not only the inhibition of PrP super(Sc) formation but also the reversal of TSE-associated neuropathology.

DESCRIPTORS: Prion protein; Scrapie; Transmissible spongiform encephalopathy; Disease transmission; Reviews; Creutzfeldt-Jakob disease; Lymphoid tissue; Infectious diseases; Bovine spongiform encephalopathy; Immunotherapy; Neuropathology SUBJ CATG: 11091, Vertebrate Nervous Systems: General

9/9/11 (Item 1 from file: 34)
DIALOG(R) File 34: SciSearch(R) Cited Ref Sci
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05787934 Genuine Article#: WX516 Number of References: 337

Title: Interleukin-6: Structure-function relationships

Author(s): Simpson RJ (REPRINT); Hammacher A; Smith DK; Matthews JM; Ward

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Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY

Abstract: Interleukin-6 (IL-6) is a multifunctional cytokine that plays a central role in host defense due to its wide range of immune and hematopoietic activities and its potent ability to induce the acute phase response. Overexpression of IL-6 has been implicated in the pathology of a number of diseases including multiple myeloma, rheumatoid arthritis, Castleman's disease, psoriasis, and post-menopausal osteoporosis. Hence, selective antagonists of IL-6 action may offer therapeutic benefits. IL-6 is a member of the family of cytokines that includes interleukin-11, leukemia inhibitory factor, oncostatin M, cardiotrophin-1 and ciliary neurotrophic factor. Like the other members of this family, IL-6 induces growth or differentiation via a receptor-system that involves a specific receptor and the use of a shared signaling subunit, gp130. Identification of the regions of IL-6 that are involved in the interactions with the IL-6 receptor and gp130 is an important first step in the rational manipulation of the effects of this cytokine for therapeutic benefit. In this review, we focus on the sites on IL-6 which interact with its low-affinity specific receptor, the IL-6 receptor, and the high-affinity converter qp130. A tentative model for the IL-6 hexameric receptor ligand complex is presented and discussed with respect to the mechanism of action of the other members of the IL-6 family of cytokines.

- Descriptors--Author Keywords: cytokine ; gp130 ; interleukin-6 ; receptor ; structure-function ; ternary complex
- Identifiers--KeyWord Plus(R): COLONY-STIMULATING FACTOR; CILIARY

  NEUROTROPHIC FACTOR; LEUKEMIA INHIBITORY FACTOR; HYBRIDOMA

  GROWTH-FACTOR; IL-6 SIGNAL TRANSDUCER; RECOMBINANT HUMAN INTERLEUKIN-6;

  NUCLEAR-MAGNETIC-RESONANCE; SITE-DIRECTED MUTAGENESIS; NEUTRALIZING

  MONOCLONAL- ANTIBODIES; 3-DIMENSIONAL SOLUTION STRUCTURE
- Research Fronts: 95-0477 012 (CYTOKINE RECEPTOR SIGNALING MECHANISMS; ACTIVATION OF MULTIPLE PROTEIN-TYROSINE KINASES; STAT TRANSCRIPTION FACTORS; EARLY RESPONSE GENES)
  - 95-0040 006 (GROWTH-HORMONE RECEPTOR; GH IN PRIMARY RAT ADIPOCYTES; CARBOXYL-TERMINAL DOMAIN)
  - 95-1841 004 (ELEVATED SOLUBLE INTERLEUKIN-6 RECEPTOR; CASTLEMANS DISEASE; SEVERE POLYNEUROPATHY OF THE POEMS SYNDROME; GIANT LYMPH-NODE HYPERPLASIA; MYELOMA CELLS)
  - 95-0089 002 (1.8 ANGSTROM RESOLUTION; CRYSTAL-STRUCTURE ANALYSIS OF 2 CRYSTAL FORMS; SECONDARY ANCHOR POSITIONS IN THE MAJOR HISTOCOMPATIBILITY COMPLEX BINDING GROOVE)
  - 95-3294 002 (TUMOR-NECROSIS-FACTOR-ALPHA IN RHEUMATOID-ARTHRITIS; MONOCLONAL- ANTIBODY THERAPY; TNF ACTION; CHRONIC INFLAMMATORY DISEASE; THERAPEUTIC PERSPECTIVE)
  - 95-7445 002 (INTERLEUKIN-6 (IL-6) AUTOANTIBODIES; MUCOSAL IMMUNITY; TUMOR-NECROSIS-FACTOR-ALPHA PRODUCTION IN HUMAN PERIPHERAL-BLOOD MONONUCLEAR-CELLS)
  - 95-0323 001 (INTERLEUKIN-12 INCREASES INTERLEUKIN-4 PRODUCTION; ESTABLISHED LEISHMANIA-MAJOR INFECTION IN MICE; TH1 CELLS; CYTOKINE THERAPY)
  - 95-0827 001 (AIDS-RELATED KAPOSIS-SARCOMA; SPINDLE CELLS; HERPESVIRUS-LIKE DNA-SEQUENCES; HUMAN-IMMUNODEFICIENCY-VIRUS TYPE-1 TAT PROTEIN)

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95-1180 001
                 (INTERLEUKIN-1 RECEPTOR ANTAGONIST; SEPTIC SHOCK;
    TUMOR-NECROSIS-FACTOR IN SEPSIS)
  95-1975 001
                (THROMBOPOIETIN INDUCES MEGAKARYOCYTE DIFFERENTIATION;
    C-MPL LIGAND; IN-VITRO GROWTH OF HUMAN HEMATOPOIETIC PROGENITOR CELLS)
                 (HUMAN-IMMUNODEFICIENCY-VIRUS INFECTION; PROINFLAMMATORY
  95-3277 001
    CYTOKINE EXPRESSION; IMMUNE CELLS; CIRCULATING INTERLEUKIN-6 RECEPTOR;
    HIV-1 DISEASE)
  95-5516 001
                 (BONE MASS; INTERLEUKIN-6 IN POSTMENOPAUSAL WOMEN;
    OSTEOBLASTIC CELLS; ESTROGEN THERAPY; EXPRESSION OF CYTOKINE ACTIVITY;
    LOCAL FACTORS)
  95-7760 001
                 (EXPANSION OF PRIMITIVE MURINE BONE-MARROW PROGENITOR CELLS
    IN-VITRO; HEMATOPOIETIC GROWTH-FACTORS; FLT3 LIGAND)
  95-8716 001
               (RECEPTOR TYROSINE KINASES; EPIDERMAL GROWTH-FACTOR;
    INTERLEUKIN-1 MODULATES PHOSPHORYLATION OF PROTEINS)
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Dealing with intractable protein cores: Protein sequencing of the Mcg IgG and the Yvo IgM heavy chain variable domains.

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ABSTRACT: The VH domains of two human monoclonal antibodies, designated Mcg IgGl(lambda) and Yvo IgM(kappa), were particularly intractable to standard protein sequencing protocols. Peptides liberated from the VH domains of these proteins, using standard enzymatic or chemical cleavages, invariably precipitated during the procedures. Boiling in SDS containing buffers dissolved precipitates and the peptides were separated using SDS-PAGE. Fully overlapped VH sequences were obtained with a series of 'in-gel' cleavages, followed by passive/differential transfers of peptides onto PVDF membranes. Both the in-gel cleavages and passive transfers could be applied to 'wet' or 'dry' gels so that gels could be archived and used at a later date to obtain additional sequence information from a fragment of interest. Repetitive yields of even the

most insoluble peptides were such that the sequences of various peptides from relatively complex mixtures of peptides could be assigned with confidence. Despite the overall success of the sequencing, we occasionally referred to electron density maps, calculated for crystals of the Fab of Yvo IgM, to resolve particular sequences and confirm ambiguous amino acid assignments. Methods we describe in this report

### should be generally useful for obtaining sequences of proteins with intractable cores and may find many applications in the 'post genomic era'. DESCRIPTORS: MAJOR CONCEPTS: Biochemistry and Molecular Biophysics CHEMICALS & BIOCHEMICALS: intractable protein cores; Mcg IgG--heavy chain variable domains; Yvo IgM heavy chain--variable domains; insoluble peptides; human monoclonal antibodies METHODS & EQUIPMENT: protein sequencing--genetic techniques, laboratory techniques; antibody crystallography -- laboratory techniques MISCELLANEOUS TERMS: electron density maps CONCEPT CODES: 10060 Biochemistry studies - General 10064 Biochemistry studies - Proteins, peptides and amino acids 11/9/2 (Item 2 from file: 5) DIALOG(R) File 5: Biosis Previews (R) (c) 2006 BIOSIS. All rts. reserv. BIOSIS NO.: 199800413038 0011618791 Preparation, purification and crystallization of antibody Fabs and single-chain Fv domains BOOK TITLE: Immunology Methods Manual, Vol. 1 AUTHOR: Sharma Sadhana (Reprint); Rose David R BOOK AUTHOR/EDITOR: Lefkovits I (Editor) AUTHOR ADDRESS: Div. Mol. Struct. Biol., Ont. Cancer Inst., Univ. Toronto, Toronto, ON, Canada \*\* Canada p15-37 1997 MEDIUM: print BOOK PUBLISHER: Academic Press, Inc., 1250 Sixth Ave., San Diego, California 92101, USA Academic Press Ltd., 14 Belgrave Square, 24-28 Oval Road, London NW1 70X, England, UK ISBN: 0-12-442711-1 DOCUMENT TYPE: Book; Book Chapter RECORD TYPE: Citation LANGUAGE: English DESCRIPTORS: MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Immune System--Chemical Coordination and Homeostasis; Methods and Techniques CHEMICALS & BIOCHEMICALS: antibody--antigen-binding fragment domain, crystallization, purification, single chain variable fragment domain, preparation METHODS & EQUIPMENT: antibody crystallization --chemical modification, protocol, synthetic method; antibody purification: antibody single chain variable fragment domain preparation--protocol,

Isolation/Purification Techniques--CB, protocol, purification method; sample preparation method, specimen preparation techniques; enzymatic antibody-binding fragment production--Synthesis/Modification Techniques synthetic method, protocol; scFv gene purification: Isolation/Purification Techniques--CB, protocol, purification method

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  10054 Biochemistry methods - Proteins, peptides and amino acids
  10504 Biophysics - Methods and techniques
  10506 Biophysics - Molecular properties and macromolecules
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CONCEPT CODES:
  00520 General biology - Symposia, transactions and proceedings
  03502 Genetics - General
  34502 Immunology - General and methods
 11/9/4
            (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0008702527
             BIOSIS NO.: 199395004793
Down-regulation of lymphocyte CD4 antigen expression by administration of
  anti-CD4 monoclonal antibody
AUTHOR: Morel P (Reprint); Nicolas J F; Wijdenes J; Revillard J P (Reprint)
AUTHOR ADDRESS: Immunol. Lab., INSERM U80, CNRS URA, 1177 Lyon, France**
JOURNAL: Clinical Immunology and Immunopathology 64 (3): p248-253 1992
ISSN: 0090-1229
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
ABSTRACT: Modulation of surface CD4 antigen expression was assessed by flow
  cytometry after calibration with 125I-labeled anti-CD4 monoclonal
  antibodies (mAbs). Three patients with severe psoriasis treated with BB14
  (anti-CD4 mouse IgG1) and five patients with rheumatoid arthritis treated
  with BL4 (anti-CD4 mouse IgG2a) were analyzed for sequential changes in
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surface CD4 expression on CD4+ blood lymphocytes. Anti-CD4 mAb treatment

induced a decrease of 50 to 80% of CD4 expression, with slow and partial recovery after cessation of mAb administration. CD4 modulation was related to mAb dosage and mAb concentration in plasma. It was achieved at nonsaturating concentration. In vitro incubation of blood monuclear cells induced CD4 modulation of similar kinetics and magnitude, associated with decrease of 5-10% of CD3 expression. CD4 modulation required both an intact Fc part of the antibody and the presence of monocytes. The possible role of CD4 modulation should be considered along with other functional activities of anti-CD4 mAbs in analyzing the mechanisms of the clinical effects of these antibodies.

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REGISTRY NUMBERS: 7553-56-2: IODINE
DESCRIPTORS:
  MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Blood and
    Lymphatics -- Transport and Circulation; Cell Biology; Clinical
    Endocrinology--Human Medicine, Medical Sciences; Dermatology--Human
    Medicine, Medical Sciences; Immune System--Chemical Coordination and
    Homeostasis; Pathology; Skeletal System--Movement and Support
  BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,
    Animalia
  ORGANISMS: human (Hominidae)
  COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates;
    Vertebrates
  CHEMICALS & BIOCHEMICALS:
                               IODINE
 MISCELLANEOUS TERMS: ANTI-CD4 MOUSE IMMUNOGLOBULIN G1; ANTI-CD4 MOUSE
    IMMUNOGLOBULIN G2A; ANTIBODY CRYSTALLIZABLE FRAGMENT; BLOOD
    MONONUCLEAR CELL; FLOW CYTOMETRY; IN-VITRO; IODINE RADIOISOTOPE;
    PSORIASIS; RHEUMATOID ARTHRITIS
CONCEPT CODES:
  02508 Cytology - Human
  06504 Radiation biology - Radiation and isotope techniques
  10064 Biochemistry studies - Proteins, peptides and amino acids
  10068 Biochemistry studies - Carbohydrates
  10504 Biophysics - Methods and techniques
  10506 Biophysics - Molecular properties and macromolecules
  12508 Pathology - Inflammation and inflammatory disease
  15002 Blood - Blood and lymph studies
  15004 Blood - Blood cell studies
  15008 Blood - Lymphatic tissue and reticuloendothelial system
  18006 Bones, joints, fasciae, connective and adipose tissue - Pathology
  18506 Integumentary system - Pathology
  22003 Pharmacology - Drug metabolism and metabolic stimulators 22005 Pharmacology - Clinical pharmacology
  22018 Pharmacology - Immunological processes and allergy
  32600 In vitro cellular and subcellular studies
  34502 Immunology - General and methods 34508 Immunology - Immunopathology, tissue immunology
BIOSYSTEMATIC CODES:
  86215 Hominidae
            (Item 5 from file: 5)
 11/9/5
DIALOG(R) File 5: Biosis Previews(R)
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0008359821

BIOSIS NO.: 199294061662

AUTHOR: STEIPE B (Reprint); PLUECKTHUN A; HUBER R

COMPLEMENTARITY-DETERMINING REGION 1-GRAFTED MUTANT

REFINED CRYSTAL STRUCTURE OF A RECOMBINANT IMMUNOGLOBULIN DOMAIN AND A

AUTHOR ADDRESS: ABT STRUKTURFORSCHUNG, MAX-PLANCK-INST BIOCHEMIE, AM

KLOPFERSPITZ, 8033 MARTINSREID, GER\*\*GERMANY

JOURNAL: Journal of Molecular Biology 225 (3): p739-753 1992

ISSN: 0022-2836

DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: ENGLISH

ABSTRACT: We report the solution of the crystal structure of a mutant of the immunoglobulin VL domain of the antibody McPC603, in which the complementarity-determining region 1 segment is replaced with that of a different antibody. The wild-type and mutant crystal structures have been refined to a crystallographic R-factor of 14.9% at a nominal resolution of 1.97 .ANG.. A detailed description of the structures is given. Crystal packing results in a dimeric association of domains, in a fashion closely resembling that of an Fv fragment. The comparison of this VL domain with the same domain in the Fab fragment of McPC603 shows that the structure of an immunoglobulin VL domain is largely independent of its mode of association, even in places where the inter-subunit contacts are not conserved between VL and VH. In all three complementarity-determining regions we observe conformations that would not have been predicted by the canonical structure hypothesis. Significant differences between the VL domain dimer and the Fab fragment in the third complementarity-determining region show that knowledge of the structure of the dimerization partner and its exact mode of association may be needed to predict the precise conformation of antigen-binding loops.

## DESCRIPTORS: ANTIBODY CRYSTALLOGRAPHY FV FRAGMENT FAB FRAGMENT ANTIGEN-BINDING LOOPS

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Genetics; Immune System--Chemical Coordination and Homeostasis; Metabolism; Molecular Genetics--Biochemistry and Molecular Biophysics

CONCEPT CODES:

03506 Genetics - Animal

03508 Genetics - Human

10010 Comparative biochemistry

10052 Biochemistry methods - Nucleic acids, purines and pyrimidines

10054 Biochemistry methods - Proteins, peptides and amino acids

10058 Biochemistry methods - Carbohydrates

10062 Biochemistry studies - Nucleic acids, purines and pyrimidines

10064 Biochemistry studies - Proteins, peptides and amino acids

10068 Biochemistry studies - Carbohydrates

10300 Replication, transcription, translation

10506 Biophysics - Molecular properties and macromolecules

13002 Metabolism - General metabolism and metabolic pathways

13004 Metabolism - Carbohydrates

13012 Metabolism - Proteins, peptides and amino acids

13014 Metabolism - Nucleic acids, purines and pyrimidines

15002 Blood - Blood and lymph studies

15008 Blood - Lymphatic tissue and reticuloendothelial system

34502 Immunology - General and methods

34508 Immunology - Immunopathology, tissue immunology

### 11/9/6 (Item 1 from file: 34)

DIALOG(R) File 34: SciSearch(R) Cited Ref Sci (c) 2006 Inst for Sci Info. All rts. reserv.

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12976304
          Genuine Article#: 838SU
                                     Number of References: 45
Title: Structural convergence of antibody binding of carbohydrate
    determinants in Lewis Y tumor antigens
Author(s): Ramsland PA (REPRINT); Farrugia W; Bradford TM; Hogarth PM;
    Scott AM
Corporate Source: Austin Res Inst, Struct Immunol Lab, Heidelberg/Vic
    3084/Australia/ (REPRINT); Austin Res Inst, Struct Immunol
    Lab, Heidelberg/Vic 3084/Australia/; Ludwig Inst Canc Res, Tumour
    Targeting Program, Heidelberg/Vic 3084/Australia/(
    p.ramsland@ari.unimelb.edu.au)
Journal: JOURNAL OF MOLECULAR BIOLOGY, 2004, V340, N4 (JUL 16), P809-818
ISSN: 0022-2836
                Publication date: 20040716
Publisher: ACADEMIC PRESS LTD ELSEVIER SCIENCE LTD, 24-28 OVAL RD, LONDON
    NW1 7DX, ENGLAND
Language: English
                  Document Type: ARTICLE
Geographic Location: Australia
Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY
Abstract: Antibodies targeting human epithelial carcinomas bearing Lewis Y
    (Le(y)) carbohydrate antigens provide a striking illustration of
    convergent immune recognition. We report a 1.9 Angstrom resolution
    crystal structure of the Fab of a humanized antibody (hu3S193) in
    complex with the Ley tetrasaccharide, Fuc(alpha1 --> 2) Gal(beta1 -->
    4) [Fuc(alpha1 --> 3)]GlcNAc. Comparisons of the hu3S193 and BR96
    antibodies bound to Ley tumor antigens revealed extremely similar
    mechanisms for recognition of the carbohydrate epitopes. Solvent plays
    a critical role in hu3S193 antibody binding to the Ley carbohydrate
    epitope. Specificity for Ley is maintained because a conserved pocket
    accepts an N-acetyl group of the core Gal(betal --> 4)GlcNAc
    disaccharide. Closely related blood-group determinants (Le(a) and
    Le(b)) cannot enter the specificity pocket, making the Ley antibodies
    promising candidates for immunotherapy of epithelial cancer. (C) 2004
    Elsevier Ltd. All rights reserved.
Descriptors--Author Keywords: antibody crystallography; cancer
    treatments; carbohydrate antigens; humanized antibody; tumor
    targeting
Identifiers--KeyWord Plus(R): 3-DIMENSIONAL STRUCTURE;
    MONOCLONAL-ANTIBODIES; FAB FRAGMENT; COMPLEX; BLOOD; RECOGNITION;
    EXPRESSION; CANCER; CRYSTALLOGRAPHY; SPECIFICITY
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# 11/9/7 (Item 2 from file: 34) DIALOG(R)File 34:SciSearch(R) Cited Ref Sci (c) 2006 Inst for Sci Info. All rts. reserv.

11205616 Genuine Article#: 619JK Number of References: 102

Title: Crystal structures of human antibodies: a detailed and unfinished tapestry of immunoglobulin gene products

Author(s): Ramsland PA (REPRINT); Farrugia W

Corporate Source: Austin Res Inst, Struct Biol Lab, Kronheimer Bldg
A&MRC, Studley Rd/Heidelberg/Vic 3084/Australia/ (REPRINT); Austin Res
Inst, Struct Biol Lab, Heidelberg/Vic 3084/Australia/

Journal: JOURNAL OF MOLECULAR RECOGNITION, 2002, V15, N5 (SEP-OCT), P 248-259

ISSN: 0952-3499 Publication date: 20020900

Publisher: JOHN WILEY & SONS LTD, BAFFINS LANE CHICHESTER, W SUSSEX P019 1UD, ENGLAND

Language: English Document Type: REVIEW

Geographic Location: Australia

Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY; BIOPHYSICS
Abstract: Sequencing of all human immunoglobulin (Ig) germline gene
segments has recently been completed. However, our first glimpses of
the recombined products of this combinatorial gene system were in the
1970s, in landmark publications, reporting the crystal structures of
two human myeloma proteins, the Meg lambda light chain dimer and the
New IgG1(lambda) Fab. Although numerous crystal structures of marine
and human antibodies have now been determined, only a relatively small
proportion of the human germline genes have had their corresponding
protein three-dimensional structures resolved. Therefore, further
structural investigations are required before the inherent diversity of
the antibody repertoire can be fatly appreciated. We discuss the
detailed structural information available for human antibodies with
regard to their immune functions. Also discussed, is how the structural

information is finding application in the 'humanization' of murine antibodies as part of their development as 'biopharmaceuticals' for the treatment of human disease. Copyright (C) 2002 John Wiley Sons, Ltd. Descriptors--Author Keywords: antibody crystallography; antibody engineering; antibody structure; humanization; human antibodies Identifiers -- KeyWord Plus(R): IMMUNODEFICIENCY-VIRUS TYPE-1; INTACT HUMAN-IMMUNOGLOBULIN; CD3 MONOCLONAL-ANTIBODY; BENCE-JONES PROTEIN; HUMAN-IGM ANTIBODY; 3-DIMENSIONAL STRUCTURE; FAB FRAGMENT; LAMBDA-TYPE; 2.8-A RESOLUTION; VARIABLE DOMAIN Cited References: ALLAZIKANI B, 1997, V273, P927, J MOL BIOL ALTSCHUH D, 1992, V256, P92, SCIENCE AMIT AG, 1986, V233, P747, SCIENCE BOLT S, 1993, V23, P403, EUR J IMMUNOL BOULIANNE GL, 1984, V312, P643, NATURE BOYD PN, 1995, V32, P1311, MOL IMMUNOL BROWN M, 2000, V191, P2101, J EXP MED BRUGGEMANN M, 1989, V170, P2153, J EXP MED BRUGGEMANN M, 1991, V21, P1323, EUR J IMMUNOL CAUERHFF A, 2000, V165, P6422, J IMMUNOL CHACKO S, 1996, V271, P12191, J BIOL CHEM CHOTHIA C, 1992, V227, P799, J MOL BIOL CLACKSON T, 1991, V352, P624, NATURE CLARK M, 2000, V21, P397, IMMUNOL TODAY CO MS, 1991, V88, P2869, P NATL ACAD SCI USA COLMAN PM, 1987, V326, P358, NATURE CORPER AL, 1997, V4, P374, NAT STRUCT BIOL DEISENHOFER J, 1976, V357, P1421, H-S Z PHYSIOL CHEM DEUTSCH HF, 1971, V190, P472, ANN NY ACAD SCI EDMUNDSON AB, 1971, V36, P427, COLD SPRING HARB SYM EDMUNDSON AB, 1995, V1, P41, ANTIBODIES EDMUNDSON AB, 1996, V9, P542, METHODS EDMUNDSON AB, 1975, V14, P3953, BIOCHEMISTRY-US EDMUNDSON AB, 1970, V245, P2763, J BIOL CHEM EDMUNDSON AB, 1974, V1, P103, PROGR IMMUNOLOGY 2 EDMUNDSON AB, 1974, V13, P3816, BIOCHEMISTRY-US ELY KR, 1978, V17, P820, BIOCHEMISTRY-US ELY KR, 1989, V210, P601, J MOL BIOL FABER C, 1998, V3, P253, IMMUNOTECHNOLOGY FAN ZC, 1992, V228, P188, J MOL BIOL FAN ZC, 1999, V12, P19, J MOL RECOGNIT FEINSTEIN A, 1965, V205, P147, NATURE FETT JW, 1973, V10, P115, IMMUNOCHEMISTRY FOOTE J, 1992, V224, P487, J MOL BIOL FUREY W, 1983, V167, P661, J MOL BIOL GRAILLE M, 2000, V97, P5399, P NATL ACAD SCI USA GREEN LL, 1994, V7, P13, NAT GENET GUDDAT LW, 1994, V236, P247, J MOL BIOL GUDDAT LW, 2000, V302, P853, J MOL BIOL GUDDAT LW, 1993, V90, P4271, P NATL ACAD SCI USA HARRIS LJ, 1998, V275, P861, J MOL BIOL HARRIS LJ, 1992, V360, P369, NATURE HE XM, 1992, V89, P7154, P NATL ACAD SCI USA HERRON JN, 1991, V11, P159, PROTEINS HSU E, 1992, V2, P422, CURR OPIN STRUC BIOL HUANG DB, 1997, V34, P1291, MOL IMMUNOL HUANG DB, 1996, V93, P7017, P NATL ACAD SCI USA HUNKAPILLER T, 1989, V44, P1, ADV IMMUNOL JONES PT, 1986, V321, P522, NATURE

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11/9/8 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2006 Inst for Sci Info. All rts. reserv.

Genuine Article#: 597YH Number of References: 19 Title: Protein L mutants for the crystallization of antibody fragments Author(s): Stura EA (REPRINT); Graille M; Housden NG; Gore MG Corporate Source: Ctr Etud Saclay, CEA, Dept Ingn & Etud Prot, F-91191 Gif Sur Yvette//France/ (REPRINT); Ctr Etud Saclay, CEA, Dept Ingn & Etud Prot, F-91191 Gif Sur Yvette//France/; Univ Southampton, Inst Biomol Sci, Dept Biochem, Southampton SO16 7PX/Hants/England/ Journal: ACTA CRYSTALLOGRAPHICA SECTION D-BIOLOGICAL CRYSTALLOGRAPHY, 2002 , V58, 10,1 (OCT), P1744-1748 ISSN: 0907-4449 Publication date: 20021000 Publisher: BLACKWELL MUNKSGAARD, 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK Language: English Document Type: ARTICLE Geographic Location: France; England Journal Subject Category: BIOCHEMICAL RESEARCH METHODS; BIOCHEMISTRY & MOLECULAR BIOLOGY; BIOPHYSICS; CRYSTALLOGRAPHY Abstract: In many cases, antibody and their complexes can be crystallized and their structure determined without major difficulties. The remaining problematic cases may be approached through techniques such as of combinatorial complex crystallization which uses immunoglobulin binding proteins (IBP). The range of lattices that can be made using this method can be expanded by engineering mutants of IBP domains. We have designed Peptostreptococcus magnus protein L (PpL) mutants with altered immunoglobulin light chain binding characteristics. While the wild type PpL has two binding sites, some of the mutants contact the light chain via only one site. Other mutants have combinations of weakened first and second binding sites that modify their crystallization properties and their packing mode. In this study, we have selected PpL mutants with different behavior and that are most useful for crystallization and we present the various packing modes obtained so far. Descriptors--Author Keywords: antibody crystallization; immunoglobulin binding protein; crystal engineering; protein L mutants Identifiers -- KeyWord Plus(R): PEPTOSTREPTOCOCCUS-MAGNUS; MACROMOLECULAR COMPLEXES; FAB FRAGMENT; ANTIGEN; RECOGNITION; DOMAIN Cited References: AREVALO JH, 1993, V231, P103, J MOL BIOL BECKINGHAM JA, 2001, V353, P395, BIOCHEM J 2 BRUNGER AT, 1998, V54, P905, ACTA CRYSTALLOGR D 5 DERRICK JP, 1999, V55, P314, ACTA CRYSTALLOGR D 1 GRAILLE M, 2001, V9, P679, STRUCTURE GRAILLE M, 2000, V97, P5399, P NATL ACAD SCI USA JOLIVETREYNAUD C, 1998, V56, P300, J MED VIROL MCREE DE, 1999, V125, P156, J STRUCT BIOL NAVAZA J, 1994, V50, P157, ACTA CRYSTALLOGR A OTWINOWSKI Z, 1997, V276, P307, METHOD ENZYMOL RINI JM, 1992, V255, P959, SCIENCE ROUSSEL A, 1989, P77, SILICON GRAPHICS GEO SHERIFF S, 1996, V259, P938, J MOL BIOL STURA EA, 2001, V232, P573, J CRYST GROWTH STURA EA, 2001, V232, P580, J CRYST GROWTH STURA EA, 2001, V232, P545, J CRYST GROWTH STURA EA, 1999, P177, CRYSTALLIZATION NUCL STURA EA, 2002, V58, P1740, ACTA CRYSTALLOGR 10

11/9/9 (Item 4 from file: 34)
DIALOG(R) File 34: SciSearch(R) Cited Ref Sci

STURA EA, 2002, V58, P1715, ACTA CRYSTALLOGR 10

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10007523 Genuine Article#: 473KL Number of References: 27

Title: The liquid protein phase in crystallization: a case study - intact immunoglobulins

Author(s): Kuznetsov YG; Malkin AJ; McPherson A (REPRINT)

Corporate Source: Univ Calif Irvine, Dept Mol Biol &

Biochem, Irvine/CA/92697 (REPRINT); Univ Calif Irvine, Dept Mol Biol & Biochem, Irvine/CA/92697

Journal: JOURNAL OF CRYSTAL GROWTH, 2001, V232, N1-4 (NOV), P30-39

ISSN: 0022-0248 Publication date: 20011100

Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS

Language: English Document Type: ARTICLE

Geographic Location: USA

Journal Subject Category: CRYSTALLOGRAPHY

Abstract: A common observation by protein chemists has been the appearance, for many proteins in aqueous solutions, of oil like droplets, or in more extreme cases the formation of a second oil like phase. These may accompany the formation of precipitate in "salting out" or "salting in' procedures, but more commonly appear in place of any precipitate. Such phase separations also occur, with even greater frequency, in the presence of polymeric precipitants such as polyethyleneglycol (PEG). In general the appearance of a second liquid phase has been taken as indicative of protein aggregation, though an aggregate state distinctly different from that characteristic of amorphous precipitate. While the latter is thought to be composed of linear and branched assemblies, polymers of a sort, the oil phase suggests a more compact, three-dimensional, but fluid state. An important property of an alternate, fluid phase is that it can mediate transitions between other states, for example, between protein molecules free in solution and protein molecules immobilized in amorphous precipitate or crystals. The "liquid protein" phase can be readily observed in many crystallization experiments either prior to the appearance of visible crystals, or directly participating in the crystal growth process. In some cases the relationship between the liquid phase and developing crystals is intimate. Crystals grow directly from the liquid phase, or appear only after the visible formation of the liquid phase. We describe here our experience with a class of macromolecules, immunoglobulins, and particularly IDEC-151, an IgG specific for CD4 on human lymphocytes. This protein has been crystallized from a Jeffamine-LiSO4 mother liquor and, its crystallization illustrates many of the features associated with the liquid protein, or protein rich phase. (C) 2001 Elsevier Science B.V. All rights reserved.

Descriptors--Author Keywords: phase transitions; nucleation; antibody crystals; proteins

Identifiers--KeyWord Plus(R): ATOMIC-FORCE-MICROSCOPY; LIGHT-SCATTERING INVESTIGATIONS; HIGH SALT CONCENTRATION; MACROMOLECULAR CRYSTALS; MONOCLONAL-ANTIBODY; POLYETHYLENE-GLYCOL; SURFACE-MORPHOLOGY; DEFECT STRUCTURE; GROWTH-KINETICS; VIRUS CRYSTALS

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## Crystal structure of a glycosylated Fab from an IgM cryoglobulin with properties of a natural proteolytic antibody

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The 2.6 A (1 A = 0.1 nm) resolution structure has been determined for the glycosylated Fab (fragment antigen binding) of an IgM (Yvo) obtained from a subject with Waldenstrom's macroglobulinaemia. Dynamic light scattering was used to estimate the gel point and monitor the formation of an ordered hydroscopic gel of Yvo IgM upon cooling. If a cryoglobulin forms gels in peripheral tissues and organs, the associated swelling and damage to microvasculature can result in considerable morbidity and mortality. The three-dimensional structure of the branched N-linked oligosaccharide associated with the CH1 domain (first constant domain of heavy chain) is reported. The carbohydrate may act to shield part of the lateral surface of the CH1 domain and crowd the junction between the CH1 and CH2 domains, thereby limiting the segmental flexibility of the Fab arms in intact Yvo IgM, especially at low temperatures. Recently, Yvo IgM was shown to have the properties of a naturally occurring proteolytic antibody [Paul, Karle, Planque, Taguchi, Salas, Nishiyama, Handy, Hunter, Edmundson and Hanson (2004) J. Biol. Chem. 279, 39611-39619; Planque, Bangale, Song, Karle, Taguchi, Poindexter, Bick, Edmundson, Nishiyama and Paul (2004) J. Biol Chem. 279, 14024-14032]. The Yvo protein displayed the ability to cleave, by a nucleophilic mechanism, the amide bonds of a variety of serine

protease substrates and the gp120 coat protein of HIV. An atypical serine, arginine and glutamate motif is located in the middle of the Yvo antigen-binding site and displays an overall geometry that mimics the classical serine, histidine and aspartate catalytic triad of serine proteases. Our present findings indicate that pre-existing or natural antibodies can utilize at least one novel strategy for the cleavage of peptide bonds. (c) 2006 Biochemical Society.

AUTHOR KEYWORDS: Antibody crystallography; Combinatorial peptide chemistry; Cryoglobulin; Glycoprotein; IgM; Natural proteolytic antibody

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